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An update on post-treatment surveillance and diagnosis of recurrence in women with gynecologic malignancies: Society of Gynecologic Oncology (SGO) recommendations

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HIGHLIGHTS

- Surveillance strategies for gynecologic cancer vary based on stage and recurrence risk.
- Review of symptoms, physical exam, and education are the most effective methods in surveillance.
- Data supports limiting/eliminating routine imaging and cytology in the surveillance period.

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ABSTRACT

Gynecologic cancers account for ~12% of all new cancer cases in women and ~15% of all female cancer survivors. Current and continued advances within the field have resulted in long-term outcomes and a high rate of survivors. Therefore determining the most cost-effective clinical surveillance for detection of recurrence is critical. Unfortunately, there has been a paucity of research regarding the most effective strategies for surveillance after patients have achieved a complete response. Currently, most recommendations are based on retrospective studies and expert opinion. Taking a thorough history, performing a thorough examination, and educating cancer survivors about concerning symptoms are the most effective methods for the detection of most gynecologic cancer recurrences. There is very little evidence that routine cytology or imaging improves the ability to detect gynecologic cancer recurrence that will impact cure or response rates to salvage therapy. This article provides an update on surveillance for gynecologic cancer recurrence in women who have had a complete response to primary cancer therapy.

1. Introduction

In 2017, gynecologic malignancies are expected to afflict approximately 107,470 women within the United States [1]. Improvements in cancer care have resulted in over 8 million female cancer survivors, and this number is expected to grow by over 25% in the next ten years [2]. As survivorship continues to grow, coordination of care between gynecologic oncologists, primary care providers, other healthcare providers (such as medical and radiation oncologists), and patients will allow for compliance with cancer follow-up care and routine health maintenance. The provision of a clear understanding of recommendations and responsibilities of appropriate surveillance will reduce unnecessary tests and, ultimately, result in cost savings. In regards to surveillance, the primary objective is to provide clinical and cost-effective practices that detect recurrence and impact survival outcomes. Acceptance of surveillance should be considered if there is utility of treatment for recurrence and decreased morbidity from both monitoring for disease recurrence and treatment. One should also consider the use of resources for conducting these tests and patients should be counseled on the benefits and pitfalls of disease monitoring, which should include the psychologic impact of surveillance programs.

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The Society of Gynecologic Oncology (SGO) published recommendations for post-treatment surveillance in 2011 with the goal of providing cost-effective strategies while maintaining oncologic outcomes [3]. These posttreatment guidelines recommended the surveillance intervals, indicated procedures/tests, and the transition back to the primary care team. Despite these data, supporting a less intensive surveillance regimen, several publications have demonstrated that more intensive surveillance continues to occur at high rates on survivors of gynecologic malignancies [4,5]. Furthermore, several additional studies have been published regarding the routine surveillance and we present an update to the original recommendations from 2011.

2. Endometrial cancer

Endometrial cancer is the most common gynecologic cancer and the fourth most common cancer in women. There will be approximately 61,380 new endometrial cancer cases and 10,920 deaths in the United States in 2017 [1]. At the time of initial diagnosis, patients commonly experience symptoms, such as abnormal or postmenopausal bleeding, which warrant further investigation with ultrasound imaging and/or endometrial sampling. The combination of symptoms and diagnostic testing results in 83% of patients being diagnosed in the early stages of the disease [6]. As a result of localized disease, 5-year survival rates exceed 95% for stage I and approach 83% overall. However, recurrence rates for patients with early-stage disease range from 2 to 15% and reach as high as 50% in advanced stages or in patients with aggressive histologic condition [6]. As many local recurrences from endometrial cancer are curable, determining the ideal time interval and diagnostic tools for surveillance of recurrent endometrial cancer that can impact survival outcomes is critical.

Typically, surveillance guidelines are more intensive the first few years after diagnosis as many studies have shown that most (70–100%) recurrences occur within 3 years after primary treatment [7–9].To date, there are no prospective studies that have evaluated the role of surveillance in endometrial cancer follow-up evaluation. Based on recommended guidelines and institutional practices, retrospective research and literature reviews comprise the best evidence that is available. The most consistently used method for surveillance is the physical examination. This alone accounts for a high rate of detection that ranges from 35 to 68% of cases [8–11].Even more striking is that the combination of physical examination alone or with review of symptoms has resulted in rates of detection that exceed 80% [11–13].Therefore, physical examination, which includes a thorough speculum, pelvic, and rectovaginal examination, should be conducted during each follow-up assessment.

The role of surveillance is based on the concept that detection of recurrences in the asymptomatic stage results in better therapeutic options and outcomes. Interestingly, even with intensive surveillance, many recurrences are detected based on the presence of symptoms, occurring in 41–83% of patients [8,9,11,14]. A common symptom, vaginal bleeding, may be indicative of a local recurrence that is often curable if it is an isolated site of disease [8,11]. Even in patients diagnosed with a distant recurrence, symptoms, such as coughing, pain, lethargy, weight loss, or headaches, are presents in ~70% of cases [8,14–16]. Survival outcomes have been evaluated on the basis of the presence or absence of symptoms at the time of recurrence. Sartori et al. reported that women who experienced a symptomatic recurrence had poorer outcomes compared to women diagnosed with asymptomatic diagnosis based on examination or imaging [9]. However, many other series have reported that the role of routine surveillance in patients with stage I endometrial cancer had no difference in survival based on the presence or absence of symptoms [8,14,16]. Of note, patients who had symptoms were undergoing the recommended follow-up evaluations, which provide an argument against the use of intensive routine surveillance. Therefore, patient education on the signs and symptoms is a critical component of posttreatment care and may lead to the early detection of recurrent disease. Although all of these studies were retrospective, they reiterate the importance of prospective trials to determine the true role and regimen for surveillance.

Because most recurrences occur at the vaginal cuff, the use of vaginal cytology has been advocated; however, many gynecologic oncologists have challenged this recommendation [9,10–15,21]. Although studies have reported that cytologic evaluation detected 25% of all recurrences; the use of cytology alone in these studies detected only 3 of the 44 (7%) recurrences [10–15]. Additionally, in a study of women with early stage disease with a low recurrence risk, Salani et al. detected all recurrences based on symptoms/clinical findings and noted that cytology did not add any clinical benefit [17]. Along these same lines, Novetsky and colleagues evaluated the role of post-operative Pap test in women who underwent hysterectomy for all stages of endometrial cancer. In their study, 51 of the 433 patients studied were diagnosed with an endometrial cancer recurrence and no recurrences were diagnosed by cytology [18]. Of note, 3% of all Pap tests were abnormal, with no diagnoses of malignancy and these abnormalities were more likely secondary to radiation changes [18]. Kiran et al. reported on 52 women with recurrent cancer and also noted the limited utility of cytology. They also noted that intensive surveillance did not improve outcomes compared to those with symptomatic recurrences [19]. Even in a study of type II endometrial cancers, in which there is a higher recurrence rate, almost half of the patients were diagnosed by examination or symptoms, and no patients were diagnosed by cytology [20]. The lack of utility is compounded by the fact that the use of vaginal cytology at each visit results in an estimated cost of $27,000 per case detected [8]. Because most recurrences at the vaginal cuff can be found on examination, routine vaginal cytology adds only significant healthcare costs without added benefit. In a recent review of SEER database looking into trends for endometrial cancer surveillance in early stage (I-II) patients, the use of vaginal cytology has declined but remains high with over 66% having cytology in 2011 [4]. Based on the aforementioned data, the SGO established guidelines for cost containment called Choosing Wisely and advocate for the elimination of the use of liquid-based cytology (Pap test) of the vaginal cuff to detect recurrent endometrial cancer [21].

Similarly to ovarian cancer, the use of cancer antigen 125 (CA-125) levels has been investigated as a marker for recurrence. Pre-treatment CA-125 levels were elevated in more than one-half of the patients with advanced stage and/or high-grade histologic endometrial cancer [3,22]. Frimer et al. reported that an elevated CA-125 level at diagnosis was significantly associated with disease recurrence and even increases by 10 U/mL in the normal range or values ≥15 U/mL were associated with disease recurrence in uterine serous carcinoma [22]. However, the role of CA-125 levels in low risk disease is negligible and one must be aware of elevated CA-125 levels secondary to other conditions, including prior radiotherapy [16]. At present, the use of CA-125 levels should not be used routinely in patients with endometrial cancer, but may be appropriate in select patients with advanced disease, serous histologic condition, or in patients who have an elevated CA-125 level before treatment.

The use of radiographic imaging has been suggested for the detection of recurrent disease. Because of low costs, chest radiographs have been advocated for the detection of asymptomatic recurrences, often on a semiannual or annual basis. The rate of detection that are found on chest radiographs ranges from 0 to 20%, and in one series, chest radiograph detected 7 asymptomatic pulmonary recurrences, accounting for 0.34% of all chest radiographs that were performed for surveillance [7–8]. Although reports of isolated pulmonary recurrences, albeit rare, may be amenable to therapies that allow for long-term survival outcomes, the routine use of chest radiographs is not recommended [15, 22]. In further evaluation of radiographic imaging for endometrial cancer surveillance, Fung Kee Fung et al. conducted a review of the literature and found that only 5–21% of asymptomatic recurrences were found by computed tomography (CT) scans [7]. Even in type II